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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,413	03/30/2001	Shigeru Yamamoto	Q63731	8678

7590 01/10/2003

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EXAMINER

STEADMAN, DAVID J

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 01/10/2003

14

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application N .

09/806,413

Applicant(s)

YAMAMOTO ET AL.

Examiner

David J. Steadman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 30 October 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-4, 11-14 and 21 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 4 is/are allowed.
- 6) ☒ Claim(s) 1-3, 11-14 and 21 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_ 6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION*****Application Status***

Claims 1-4, 11-14, and 21 are pending in the application.

Applicants' amendment to claims 1, 3, 4, 11, 13, and 14, cancellation of claims 5-10 and 15-20, and addition of claim 21 in Paper No. 12, filed 10/30/02, is acknowledged.

Applicants' arguments presented in Paper No. 12 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

***Claim Rejections - 35 USC § 112, Second Paragraph***

1. In view of applicants' clarification of the term "having an activity to act upon a disaccharide glycoside to release saccharides from said disaccharide glycoside in disaccharide unit" (see pages 8-10 of Paper No. 12), rejection of claims 1, 3, 11 (claim 12 dependent therefrom), and 13, is withdrawn. While the specification indicates that the diglycosidase can cleave disaccharides into monosaccharides, applicants have clarified that this activity of the recited enzymes or polypeptides is in addition to the activity of cleaving disaccharides. Furthermore, it is clear from the claim as to the intended activity, i.e., releasing a disaccharide unit from a disaccharide glycoside.

2. Claims 1-3 and 11-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. The rejection of claim 2 as being indefinite in the recitation of "analogous disaccharide glycoside" is maintained. The rejection was fully explained in a previous Office action. Applicants argue (beginning at page 10 of Paper No. 12) the term is sufficiently defined such that a skilled artisan would recognize the scope of intended glycosides. Applicants argue the intended

"analogous disaccharide glycoside" has glucose on the aglycon side as indicated in the specification at page 6. Applicants argue the specification has been amended to clarify the dissacharide as a disaccharide glycoside having glucose on the aglycon side. Applicants' argument is not found persuasive. It is noted that applicants' amendment to the specification does not appear to be new matter as it is clear from the specification that the "disaccharides having glucose on the aglycon side" are dissacharide glycosides as the specification states, "[t]he dissacharide glycosides analogous to beta-primeverosidase are disaccharides having glucose on the aglycon side" (underline added for emphasis; page 6 of the instant specification). While the specification clearly indicates the saccharide of the disaccharide in nearest proximity to the aglycon side is glucose, the specification has provided no definition as to the saccharide that is at the X position of the disaccharide of the figure presented at page 11 of Paper No. 12. As such, one of skill in the art would not recognize the scope of applicants' intended "analogous disaccharide glycoside". While applicants have provided examples of disaccharides that are to be considered analogous to beta-primeverosidase, the claim is not so limited to these disaccharides, and in accordance with MPEP 2111, the term has been provided its broadest reasonable interpretation.

b. Claims 1 (claim 2 dependent therefrom) and 11 (claims 12-14 dependent therefrom) are indefinite in the recitation of "a substantial activity". Neither the specification nor the claims provides a definition of the term and it is unclear as to the level of enzymatic activity that applicants intend as being "substantial". It is suggested that applicants clarify the meaning of the term.

***Claim Rejections - 35 USC § 112, First Paragraph***

3. Claims 1, 2, and 11-14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the

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claimed invention. This is a new matter rejection and is necessitated by amendment. Claims 1 (claim 2 dependent therefrom) and 11 (claims 12-14 dependent therefrom) recite the limitation "wherein said enzyme has a substantial activity even at a pH 3 or less and is stable at 50°C or less". While the examiner can find support in the specification at page 50, line 2 for the limitation of "stable at 50°C or less", the examiner can find no support in the specification, claims, or figures as originally filed for the limitation of "has a substantial activity even at a pH 3 or less". It is noted that the specification has support for a limitation of an enzyme being stable at pH 3 or more (see page 50, line 2 of the instant specification).

4. The written description rejection of claims 1-3 and 11-14 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons described below. The rejection was fully explained in a previous Office action. Regarding the genus of claimed or recited enzymes and polypeptides, applicants argue the genus of claimed or recited enzymes and polypeptides are described by their function and other relevant identifying characteristics of substrate specificity and pH and temperature tolerance. Applicants' argument is not found persuasive. It is noted that the polypeptides as recited in claims 3 and 21 are not so limited to a particular substrate or to those relevant identifying characteristics of pH and temperature tolerance as recited in claims 1 and 11. The specification provides only two representative species of such enzymes or polypeptides, i.e., a mature diglycosidase having an amino acid sequence of SEQ ID NO:8 and an inactive precursor diglycosidase of SEQ ID NO:10 (SEQ ID NO:8 with an additional 22 amino acids at the N-terminus), both isolated from a single microorganism, *Aspergillus fumigatus*. The specification does not provide other representative species of the genus of claimed or recited enzymes or polypeptides. The structures of the recited genus of enzymes or polypeptides have not been adequately described in the specification. The CAFC in *UC California v. Eli Lilly*, (43 USPQ2d 1398) stated that: "In claims to genetic material, however a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA", without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others."

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One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus". Similarly with the claimed genus of proteins the functional definition of the genus does not provide any structural information commonly possessed by members of the genus, which distinguish the protein species within the genus from other proteins such that one can visualize or recognize the identity of the members of the genus. While the recited enzymes and polypeptides are described by their function and, in the case of the enzymes of claims 1 and 11, the relevant identifying characteristics of having activity at pH 3 or less and stability at 50 degrees Celsius or less, these characteristics are insufficient to describe the recited genus in such a way that a skilled artisan would recognize that applicants were in possession of the claimed invention. One of skill in the art, based on these characteristics alone, would not be able to visualize the structures of the genus of recited enzymes or polypeptides. As such, the genus of recited enzymes or polypeptides has not been adequately described in the specification.

Regarding the genus of microorganisms, applicants argue the specification supports a wide range of microorganisms. Applicants argue the specification has identified four strains exhibiting diglycosidase activity – a single strain of *A. fumigatus* and three strains of *A. niger* and have produced diglycosidase using *A. fumigatus* and *A. niger* (Examples 1 and 2). Applicants argue that diglycosidase activity was additionally identified in other molds, and a yeast, bacteria, and an actinomycetes as shown in Example 5. Applicants' argument is not found persuasive. It is noted that the genus of microorganisms as recited in the claims are not limited to those as described in Example 5 of the specification. The species of microorganisms as disclosed in the specification are not a sufficient number of representative species of the recited genus sufficient to adequately describe the genus of microorganisms. A representative number of species is inversely related to the skill and knowledge in the art. Applicants allege that at the time of the invention, microorganisms producing such enzymes were not known in the art. Thus, because there is no prior knowledge of such microorganisms in the prior art, the specification has not provided a representative number of microorganisms sufficient to describe the recited genus.

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Given this lack of description of representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

To the extent the rejection applied to the genus of substances which induce production of an enzyme as recited in original claim 13, the rejection is withdrawn. The term "substance which induces production of an enzyme" has been amended to recite "a saccharide" and applicants have utilized a variety of saccharides, which all exhibit the ability to induce diglycosidase activity in *A. fumigatus* and *A. niger* (see pages 33 and 34).

5. The scope of enablement rejection of claim 1-3, 11-14, and 21 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons described below. The rejection was fully explained in a previous Office action. Applicants argue the rejection should be withdrawn for the reasons set forth in their argument addressing the written description rejection. Applicants' argument is not found persuasive. The examiner has addressed applicants' arguments to the extent said arguments apply to the instant rejection. The examiner has interpreted applicants' arguments addressing the written description rejection to apply to enabling the entire scope (and not describing the entire genus) of recited enzymes or polypeptides, microorganisms, or inducers. Regarding the scope of claimed or recited enzymes and polypeptides, applicants argue the scope of claimed or recited enzymes and polypeptides are described by their function, substrate specificity and pH and temperature tolerance. Regarding the genus of microorganisms, applicants argue the specification supports a wide range of microorganisms. Applicants argue the specification has identified four strains exhibiting diglycosidase activity – a single strain of *A. fumigatus* and three strains of *A. niger* and have produced diglycosidase using *A. fumigatus* and *A. niger* (Examples 1 and 2). Applicants argue that diglycosidase activity was additionally identified in other molds, and a yeast, bacteria, and an actinomycetes (Example 5; see particularly page 45 of the instant specification). Applicants argue claim 13 has been amended to indicate the "substance" of original claim 13 is "a saccharide" and claim 14 has been amended to recite specific saccharides. Applicants' arguments as they apply to the enzymes, polypeptides, and microorganisms are not found persuasive. To

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the extent applicants' arguments apply to the saccharide, the rejection is withdrawn. It is noted that the polypeptides as recited in claims 3 and 21 are not so limited to a particular substrate or to those characteristics of pH and temperature tolerance as recited in claims 1 and 11 and the microorganism as recited in the claims is not limited to those as disclosed in Example 5 of the specification. Undue experimentation would be required to make the broad scope of enzymes, polypeptides, and microorganisms as recited in the claims. Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s). While the specification suggests that diglycosidase activity is present in other microorganisms, the specification provides no guidance or working examples for isolating the entire scope of recited enzymes having an activity at *any* pH less than 3 or stability at *any* temperature of 50 degrees Celsius or less. Furthermore, the specification provides guidance and a working example only for the purification of the diglycosidase from *A. fumigatus* having an amino acid sequence of SEQ ID NO:8 and neither the specification nor the prior art provide any indication that all diglycosidases from other microorganisms can be isolated using a similar procedure. Also, the specification provides guidance for isolating the nucleic acid encoding a beta-primeverosidase from *A. fumigatus* as shown in SEQ ID NO:8, however, the specification provides no indication that all structures of diglycosidases from other microorganisms will share sufficient identity such that structure-based gene isolation methods such as hybridization and PCR can be used to isolate nucleic acids encoding the entire scope of recited diglycosidase genes. Without such guidance, one of skill in the art recognizes the high degree of unpredictability in making the entire scope of recited polypeptides.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including *all* diglycosidases, methods of producing diglycosidases by culturing *any* microorganism

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in a nutrient medium that contains *any* substance that induces production of an enzyme having diglycosidase activity. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re* Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re* Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

***Claim Rejections - 35 USC § 102/103***

6. In view of applicants' remarks and amendment, rejection of claims 2 and 14 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over McCormack et al. (Biotechnol Lett 13:677-682, 1991) is withdrawn. Applicants have clarified the "analogous disaccharide glycoside" of claim 2 to a disaccharide having glucose proximal to the aglycon (see page 6, bottom paragraph). As chitin is a homopolymer of N-acetyl-D-glucosamine, chitin would not meet the limitations of an "analogous disaccharide glycoside" as recited in claim 2 or the saccharides for enzyme induction of claim 14.

7. In view of applicants' remarks and amendment, rejection of claims 1, 2, 11, 13, and 14 under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Harman et al. (US Patent 6,020,540) is withdrawn. Applicants have clarified the "analogous disaccharide glycoside" of claim 2 to a disaccharide having glucose proximal to the aglycon (see page 6, bottom paragraph). As chitin is a homopolymer of N-acetyl-D-glucosamine, chitin would not meet the limitations of an "analogous disaccharide glycoside" as recited in claim 2 or the saccharides for enzyme induction of claim 14. Also, Harman does not teach or suggest that their enzyme is active at a pH of 3 or less.

8. The rejection of claims 1, 3, and 11-13 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over McCormack et al. (Biotechnol Lett 13:677-682, 1991) is maintained for the reasons of record and the reasons described below. The amendment to claims 1 and 11 have introduced the limitation of the enzyme having a substantial activity even at pH 3 or

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less and stability at 50 degrees Celsius or less. McCormack teaches that their enzyme has activity at a pH of from 3 to 6.5 and 20-80 degrees Celsius (page 680). The rejection as it applied to the original claims was fully explained in a previous Office action. Applicants argue (beginning at page 15 of Paper No. 12) McCormack does not anticipate or render obvious the claimed enzyme, polypeptide, or methods of production thereof as, applicants allege, chitin is not a glycoside. Applicants argue the claimed invention uses a glycoside as a substrate and acts upon the bonding site between an aglycon and a saccharide chain to release saccharides in a disaccharide unit. Applicants' argument is not found persuasive. It is noted that the claims are not so limited to an enzyme, polypeptide, or method of production thereof that acts upon the bonding site between an aglycon and a saccharide chain to release saccharides in a disaccharide unit. Regarding applicants' argument alleging that chitin is not a glycoside, the definition of "glycoside" appears to be used loosely in the art and there is no indication in the specification that applicants' intended meaning of the term "glycoside" is a glycosidic linkage between a saccharide and an aglycon (non-saccharide moiety). For example, Voet et al. (Biochemistry, 2<sup>nd</sup> Ed., 1995, John Wiley and Sons, Inc., New York) define a glycoside as being monosaccharides held together by a glycosidic bond (page 256, right column). Solomons (Fundamentals of Organic Chemistry, 3<sup>rd</sup> Ed., 1990, John Wiley and Sons, Inc., New York) defines glycoside as carbohydrate acetals (page 862, top). Furthermore, the American Heritage Dictionary (4<sup>th</sup> Ed., 2000) indicates that chitin is a glycoside. Therefore, based on the definitions of glycoside provided in the art, one of ordinary skill in the art would recognize chitin as being a "glycoside". Thus, in accordance with MPEP 2111, directing the examiner to interpret claims in their broadest reasonable interpretation, the reference of McCormack anticipates or renders obvious claims 1, 3, and 11-13.

9. The rejection of claim 3 under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Harman et al. (US Patent 6,020,540) is maintained. The rejection was fully explained in a previous Office action. Applicants argue (beginning at page 16 of Paper No. 12) Harman does not anticipate or render obvious the claimed enzyme, polypeptide, or methods of production thereof as, applicants allege, chitin is not a glycoside. Applicants argue the claimed invention uses a glycoside as

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a substrate and acts upon the bonding site between an aglycon and a saccharide chain to release saccharides in a disaccharide unit. Applicants' argument is not found persuasive. It is noted that the claims are not so limited to an enzyme, polypeptide, or method of production thereof that acts upon the bonding site between an aglycon and a saccharide chain to release saccharides in a disaccharide unit. Regarding applicants' argument alleging that chitin is not a glycoside, as stated above, the definition of "glycoside" appears to be used loosely in the art and it appears that chitin would be considered a glycoside by one of ordinary skill in the art. Therefore, in accordance with MPEP 2111, directing the examiner to interpret claims in their broadest reasonable interpretation, the reference of Harman anticipates or renders obvious claim 3.

### **Conclusion**

10. Claims 1-3, 11-14, and 21 are rejected.

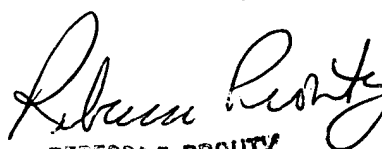
11. Claim 4 is in a condition for allowance.

Amendment to claims 1 and 11 necessitated the new grounds of rejection set forth in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Thursday from 6:30 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for this Group is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.  
Patent Examiner  
Art Unit 1652

  
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